

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

- 1           1. (Original) A nucleic acid encoding a Diphtheria toxin fusion protein  
2 comprising
  - 3                 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator;  
5 and
    - 6                 (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically  
7 binds to a protein overexpressed on the surface of a cell.
- 1           2. (Original) The nucleic acid of claim 1, wherein the matrix  
2 metalloproteinase is selected from the group consisting of MMP-2 (gelatinase A), MMP-9  
3 (gelatinase B) and membrane-type1 MMP (MT1-MMP).
- 1           3. (Original) The nucleic acid of claim 1, wherein the plasminogen activator  
2 is selected from the group consisting of tissue plasminogen activator (t-PA) and urokinase  
3 plasminogen activator (u-PA).
- 1           4. (Currently Amended) The nucleic acid of claim 1, wherein the matrix  
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ (SEQ ID  
3 NO: 20).
- 1           5. (Original) The nucleic acid of claim 1, wherein the plasminogen activator  
2 cleavage site is selected from the group consisting of QRGRSA, GSGRSA and GSGKSA.
- 1           6. (Original) The nucleic acid of claim 1, wherein the protein overexpressed  
2 on the surface of a cell is a receptor.

1               7. (Original) The nucleic acid of claim 1, wherein the heterologous  
2 polypeptide comprises a cytokine.

1               8. (Original) The nucleic acid of claim 1, wherein the heterologous  
2 polypeptide comprises a growth factor.

1               9. (Original) The nucleic acid of claim 1, wherein the heterologous  
2 polypeptide is a member selected from the group consisting of: IL-2, GM-CSF, and EGF.

1               10. (Original) The nucleic acid of claim 1, comprising the nucleotide  
2 sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

1               11. (Original) A vector comprising the nucleic acid of claim 1.

1               12. (Original) The nucleic acid of claim 6, wherein the cell is a cancer cell.

1               13. (Original) The nucleic acid of claim 7, wherein the heterologous  
2 polypeptide comprises GM-CSF.

1               14. (Original) The nucleic acid of claim 7, wherein the heterologous  
2 polypeptide comprises IL-2.

1               15. (Original) The nucleic acid of claim 8, wherein the heterologous  
2 polypeptide comprises EGF.

1               16. (Original) A nucleic acid encoding a Diphtheria toxin fusion protein  
2 comprising

3                             (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a urokinase a plasminogen activator; and

5                             (2) GM-CSF.

1               17. (Original) A polypeptide encoded by the nucleic acid of claim 1.

- 1               18. (Original) A polypeptide encoded by the nucleic acid of claim 10.
- 1               19. (Original) A polypeptide encoded by the nucleic acid of claim 16.
- 1               20. (Original) A host cell comprising the vector of claim 11.
- 1               21. (Original) The nucleic acid of claim 12, wherein the cancer is leukemia.
- 1               22. (Original) The nucleic acid of claim 12, wherein the cancer is acute  
2 myelogenous leukemia.
- 1               23. (Original) A pharmaceutical composition comprising the protein of claim  
2 18 and a pharmaceutically acceptable carrier.
- 1               24. (Original) A method of treating cancer, the method comprising  
2 administering to a subject a Diphtheria toxin fusion protein comprising  
3               (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator;  
5 and  
6               (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically  
7 binds to a protein overexpressed on the surface of a cell.
- 1               25. (Original) The method of claim 24, wherein the matrix metalloproteinase  
2 is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and  
3 membrane-type1 MMP (MT1-MMP).
- 1               26. (Original) The method of claim 24, wherein the plasminogen activator is  
2 selected from the group consisting of t-PA and u-PA.
- 1               27. (Currently Amended) The method of claim 24, wherein the matrix  
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ (SEQ ID  
3 NO: 20).

1               28. (Currently Amended) The method of claim 24, wherein the plasminogen  
2 activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23),  
3 GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1               29. (Original) The method of claim 24, wherein the protein overexpressed on  
2 the surface of a cell is a receptor.

1               30. (Original) The method of claim 24, wherein the cell is a cancer cell.

1               31. (Original) The method of claim 24, wherein the heterologous polypeptide  
2 comprises a cytokine.

1               32. (Original) The method of claim 24, wherein the heterologous polypeptide  
2 comprises a growth factor.

1               33. (Original) The method of claim 24, wherein the fusion protein is encoded  
2 by the nucleotide sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

1               34. (Original) The method of claim 30, wherein the cancer is leukemia.

1               35. (Original) The method of claim 30, wherein the cancer is acute  
2 myelogenous leukemia.

1               36. (Original) The method of claim 31, wherein the heterologous polypeptide  
2 comprises GM-CSF.

1               37. (Original) The method of claim 31, wherein the heterologous polypeptide  
2 comprises IL-2.

1               38. (Original) The method of claim 32, wherein the heterologous polypeptide  
2 comprises EGF.

1               39. (Original) The method of claim 24, wherein the Diphtheria toxin fusion  
2 protein comprises:

3               (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a urokinase plasminogen activator; and  
5               (2) GM-CSF.

1               40. (Original) A method of targeting a compound to a cell overexpressing a  
2 cytokine receptor or a growth factor receptor, the method comprising the steps of:

3               administering to the cell Diphtheria toxin fusion protein comprising  
4               (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
5 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator and  
6 wherein the Diphtheria toxin is cleaved by a matrix metalloproteinase or a plasminogen  
7 activator; and

8               (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically  
9 binds to a cytokine receptor or a growth factor receptor.

1               41. (Original) The method of claim 40, wherein the cell also overexpresses a  
2 matrix metalloproteinase, a tissue plasminogen activator, or a urokinase plasminogen activator.

1               42. (Original) The method of claim 40, wherein the matrix metalloproteinase  
2 is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and  
3 membrane-type1 MMP (MT1-MMP).

1               43. (Original) The method of claim 40, wherein the plasminogen activator is  
2 selected from the group consisting of t-PA and u-PA.

1               44. (Currently Amended) The method of claim 40, wherein the matrix  
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ SEQ ID  
3 NO: 20).

1               45. (Currently Amended) The method of claim 40, wherein the plasminogen  
2 activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23),  
3 GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1               46. (Original) The method of claim 40, wherein the cancer cell is a leukemia  
2 cell.

1               47. (Original) The method of claim 40, wherein the cancer cell is an acute  
2 myelogenous leukemia cell.

1               48. (Original) The method of claim 40, wherein the Diphtheria toxin fusion  
2 protein comprises

3               (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a urokinase plasminogen activator; and  
5               (2) GM-CSF.

1               49. (Original) An isolated nucleic acid comprising the sequence set forth in  
2 any one of SEQ ID NOS: 2-18.